Remarks

The Office Action mailed October 9, 2007, has been received and reviewed. Claims 1, 2, 5, 6, 8, 10, 17, 19, 20, 27, and 43 having been amended, claims 4, 11-16, 25, 28-42, and 44-47 having been canceled, without prejudice, the pending claims are claims 1-3, 5-10, 17-24, 26, 27, and 43. Claims 1, 5, 27, and 43 being withdrawn for examination, as drawn to non-elected inventions, the claims currently under examination are claims 2, 3, 6-10, 17-24, and 26. Reconsideration and withdrawal of the rejections are respectfully requested.

Oath/Declaration

The Examiner expressed concern that the Declaration executed by Andrew Mellor was defective, as corrections were not initialed and dated. A replacement Declaration is being executed by Andrew Mellor and will be provided to the U.S. Patent and Trademark Office as soon as it is available.

Restriction Requirement

Applicants thank the Examiner for the rejoinder and examination of claims 2, 3, 6-10, and 17-26 along with the elected claims of Group IX. Applicants continue to request the rejoinder and examination of Group I (amended claim 1 and dependent claim 5), Group II (amended claim 27), and Group X (amended claim 43) with elected Group IX. Applicants continue to submit that the burden to search and examine the methods of Groups I, II, and X along with Group IX is not unduly burdensome. Rejoinder and examination of the claims of Groups I, II, and X along with the claims of IX is respectfully requested.

In maintaining the restriction requirement, the Examiner asserted that "claims drawn to 'augmenting the rejection of tumor cells' and 'stimulating an immune response' are distinct from methods of treating cancer. The methods of treating cancer as instantly claimed require

administration to a subject and require that the subject have cancer. However, claims drawn to methods of augmenting tumor rejection or method[s] of stimulating an immune response are not limited to malignant tumors. As such, the search required for these methods is broader than that required for cancer" (page 2, Office Action mailed October 9, 2007). Applicants do not understand this assertion. Elected Group IX is drawn to a "method of delaying the relapse or progression of a tumor in a subject," not a method of treating cancer, as asserted by the Examiner The Examiner has placed methods "of treating a subject suffering from a neoplastic condition," that is, a method of treating cancer, (see claim 43) in separate restriction Group X. Thus, the Examiner's assertion that the present claims are drawn to methods of treating cancer is incorrect, as the Examiner has restricted between methods of "delaying the relapse or progression of a tumor in a subject" (Group IX, claims currently under examination) and methods "of treating a subject suffering from a neoplastic condition" (cancer).

Amended claim 1 is drawn to a "method of augmenting rejection of tumor cells by a subject, the method comprising administering to the subject an effective amount of a pharmaceutical composition comprising a D isomer of an inhibitor of indoleamine-2,3-dioxygenase," amended claim 27 is drawn to a "method of stimulating an immune response to a tumor in a subject, the method comprising administering to the subject an effective amount of a pharmaceutical composition comprising a D isomer of an inhibitor of indoleamine-2,3-dioxygenase," and amended claim 43 is drawn to "method of treating a subject suffering from a neoplastic condition, the method comprising administering to the subject an effective amount of a pharmaceutical composition comprising a D isomer of an inhibitor of indoleamine-2,3-dioxygenase." As amended, all claims involve the administration of a D isomer of an inhibitor of indoleamine-2,3-dioxygenase to a subject with a tumor (claims 1, 4, 5, and 27) or a neoplastic condition (claim 43). Thus, Applicants submit that the restriction of Group IX from Groups I, II, and X is moot. Further, the Examiner is directed to page 16, lines 7-17 of the specification, which states, "[a]s used herein, 'tumor' refers to all types of cancer, neoplasm, or malignant

tumors found in mammals." Further, '[t]he efficacy of treatment of a tumor may be assessed by any of various parameters well known in the art. This includes, but is not limited to, determinations of a reduction in tumor size, [and] determinations of the inhibition of growth" (page 16, lines 18-23 of the specification). The rejoinder and examination of the claims 1, 4, 5, 27 and 43 (Groups I, II and X) along with the claims of IX is respectfully requested.

The 35 U.S.C. §102 Rejection

The Examiner rejected claims 2-3, 6-10, 17-24, and 26 under 35 U.S.C. 102(b) as being anticipated by WO 00/66764. This rejection is traversed. According to MPEP § 2131 a "claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Independent claim 2 and dependent claims 3, 6-10, 17-24, and 26 are drawn to a "method of delaying the relapse or progression of a tumor in a subject, the method comprising administering an effective amount of a pharmaceutical composition comprising ***an isolated D isomer*** of an inhibitor of indolcamine-2,3-dioxygenase." ***WO 00/66764 does not teach D isomers*** of inhibitors of indoleamine-2,3-dioxygenase ***and does not teach administering isolated D isomers*** of inhibitors of indoleamine-2,3-dioxygenase in methods of delaying relapse or progression of a tumor in a subject. Thus, the disclosure of WO 00/66764 does not set forth each and every element of claims 2-3, 6-10, 17-24, and 26. Withdrawal of this rejection under 35 U.S.C. §102(b) is respectfully requested.

Double Patenting Rejection

Claims 6-10, 17-24, and 26 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over pending claims 1-13, 30, 31, 33 and 36 of copending Application No. 10/780,797. This rejection is traversed.

Instant claims 6-10, 17-24, and 26 all depend from independent claim 2 and are drawn to methods "of delaying the relapse or progression of a tumor in a subject, the method comprising administering an effective amount of a pharmaceutical composition comprising an isolated D

isomer of an inhibitor of indoleamine-2,3-dioxygenase." Applicants submit that claims 1-10, 13, 30, 31, 33, and 36 of copending Application No. 10/780,797 provide no teachings of D isomers of an inhibitor of indoleamine-2,3-dioxygenase. Only claims 11 and 12 of copending Application No. 10/780,797 contain a recitation of D isomers of an inhibitor of indoleamine-2,3-dioxygenase. Withdrawal of this rejection of claims 6-10 and 17-26 under the judicially created doctrine of obviousness-type double patenting over pending claims 1-10, 13, 30, 31, 33, and 36 of copending Application No. 10/780,797 is requested.

Further, present claims 6-10, 17-24, and 26 are drawn to a "method of delaying the relapse or progression of a tumor in a subject," while claims 1-10, 13, 30, 31, 33, and 36 of copending Application No. 10/780,797 are drawn to "methods of treating cancer." In the present application, in a Restriction Requirement mailed November 21, 2006, the Examiner placed the currently pending claims, drawn to a "method of delaying the relapse or progression of a tumor in a subject into Restriction Group IX and claims drawn to "methods of treating a neoplastic condition," (that is, methods of treating a subject with cancer) into restriction Group X. Applicants respectfully submit that the Examiner has placed claims drawn to the current method and claims drawn to methods of treating cancer into separate restriction groups. If this restriction requirement is maintained, Applicants respectfully remind the Examiner that it is inappropriate to reject claims on the ground of nonstatutory obviousness-type double patenting when the U.S. Patent Office has issued a Restriction Requirement restricting the claims of the present application and the claims of the co-pending application into different restriction groups.

Reconsideration and withdrawal of this provisional rejection of claims 6-10, 17-24, and 26 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14, 19, 24-31, 33 and 36 of copending Application No. 10/780,797 is requested.

The 35 U.S.C. §112, First Paragraph, Enablement Rejection

The Examiner rejected claims 2-10, 17-24, and 26 under 35 U.S.C. 112, first paragraph, because the specification, does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection is respectfully traversed.

"The present invention includes the unexpected finding that the administration of a non-physiologic D-isomer of an IDO inhibitor, including the D isomer of 1-methyl-tryptophan, results a delay in the relapse or progression of a tumor in a subject, in comparison to the administration of either the physiologic L-isomer or a DL-racemic mixture" (page 15, lines 1-4 of the specification). Independent claim 2 (and dependent claims 3, 5-10, 17-24, and 26) are drawn to a "method of delaying the relapse or progression of a tumor in a subject, the method comprising administering an effective amount of a pharmaceutical composition comprising an isolated D isomer of an inhibitor of indoleamine-2,3-dioxygenase."

Thus, Applicants do not understand the Examiner's assertions that "[t]he invention relates to the treatment of cancer and inhibition of tumor growth comprising administering an inhibitor of indoleamine-2,3-dioxygenase ***in combination with a therapeutic agent***" (see page 15 of the Office Action mailed October 9, 2007 (emphasis added)); that "[t]he claims vary in breadth; some (such as claim 1) vary broadly, reciting the treatment of cancer generally with any inhibitor of IDO in combination with any chemotherapeutic agent. . . . All [claims] . . . disclose the general treatment of cancer and tumors with the same combination of compounds, ***wherein such combination must be synergistic***" (see page 17, Office Action mailed October 9, 2007 (emphasis added)); that "a combination of an inhibitor of indoleamine-2,3-dioxygenase and a chemotherapeutic agent could be predictably used as a ***synergistic treatment***" (see page 18, Office Action mailed October 9, 2007 (emphasis in original)); and that [t]here is limited guidance in the specification with respect to what particular inhibitor of indoleamine-2,3-dioxygenase/chemotherapeutic ***combinations would be synergistic*** (see page 19, Office Action mailed October 9, 2007 (emphasis added)). Applicants respectfully submit that these statements

do not properly reflect the presently claimed invention, methods of delaying the relapse or progression of a tumor in a subject comprising administering a D isomer of an inhibitor of indoleamine-2,3-dioxygenase. Thus, the Examiner's arguments, based on a showing of synergy with the administration of an inhibitor of IDO and a chemotherapeutic agent are not relevant to the enablement of the presently claimed methods. Reconsideration and withdrawal of this rejection under 35 U.S.C. 112, first paragraph, is requested.

As amended, independent claim 2 (and dependent claims 3, 5-10, 17-24, and 26) are draw to methods comprising administering of an isolated D isomer of an inhibitor of indoleamine-2,3-dioxygenase (IDO) selected from 1-methyl-tryptophan, β-(3-benzofuranyl)-alanine, β-(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan. Applicants submit that the specification is fully enabling for the claimed methods. Reconsideration and withdrawal of this rejection under 35 U.S.C. 112, first paragraph, is requested.

Citing Muller et al. (*Expert Opin Ther Targets* (2005) 9(4):831-849), the Examiner asserted "it is clear that not all chemotherapeutic agents will be 'cooperative' with inhibition of indoleamine-2,3-dioxygenase in the treatment of cancer" (page 16 of Office Action mailed March 28, 2007). As discussed above, Applicants submit that this assertion is not relevant to the presently claimed methods.

Illustrative of the state of the art in the treatment of cancer, the Examiner cites Gura et al. (*Science* 1997, 278:1041-1042) and Johnson et al. (*British J. Cancer* 2001, 84(10):1424-1431) (bridging pages 15-16 of Office Action mailed October 9, 2007). The present application has a priority date of April 1, 2003. Applicants submit that the teachings of Gura et al. and Johnson et al. have no relevance to the present invention. As acknowledged by the Examiner, both Gura et al. and Johnson et al. pertain to the screening of candidate compounds for the identification of new agents that are effective for the treatment of cancer. The present claims are drawn to methods "of delaying the relapse or progression of a tumor in a subject . . . comprising administering . . . ***an isolated D isomer*** of an inhibitor of indoleamine-2,3-dioxygenase." Issues associated with identifying new candidate agents for the treatment of cancer have no relevance

to the presently claimed methods, all of which include the administration of a D isomer of an inhibitor of indoleamine-2,3-dioxygenase.

In view of the above discussion, reconsideration and withdrawal of this rejection of claims 2-10, 17-24, and 26 under 35 U.S.C. §112, first paragraph, as not enabled by the specification is requested.

The 35 U.S.C. §112, First Paragraph, Written Description Rejection

The Examiner rejected claims 2-3, 6-10, 17-24, and 26, under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. This rejection is respectfully traversed.

The Examiner rejected claims 2, 3, 6-10, 17-24, and 26, asserting that the specification fails to provide adequate written description for the recitation "an inhibitor of indoleamine-2,3-dioxygenase" (page 4, Office Action mailed October 9, 2007). Applicants respectfully disagree. Applicants submit that "compounds that serve as . . . inhibitors of the IDO enzyme are . . . well known" (page 15, lines 14-15 of the specification) to those of skill in the art. See also, for example, the lengthy description of inhibitors of indoleamine-2,3-dioxygenase listing in WO 00/66764 (page 6, line 21 to page 12, line 32). However, to expedite prosecution, claim 2 has been amended to recite "an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β-(3-benzofuranyl)-alanine, β-(3-benzo(b)thienyl)-alanine, 6-nitro-D-tryptophan, and combinations thereof." Applicant reserve the right to continue the prosecution of canceled subject matter in related applications.

The Examiner rejected claims 20-24 and 26, asserting that the specification fails to provide adequate written description for the recitation "vaccine[s]" (page 9, Office Action mailed October 9, 2007), and claim 23, asserting that the specification fails to provide adequate written description for the recitation "genetically modified tumor cells or genetically modified cell lines" (see page 11, Office Action mailed October 9, 2007). Applicants respectfully disagree.

"To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention" (M.P.E.P. § 2163). There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed (Wertheim, 541 F.2d at 262, 191 USPQ at 96) and, generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification. See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986)(M.P.E.P. § 2163).

Applicant submits that the level of skill in the art at the time of the present invention was very high and that vaccines, genetically modified tumor cells, and genetically modified cell lines were well understood and widely used by the skilled artisan. Further, Applicants submit that the specification describes a representative sampling of the vaccines, genetically modified tumor cells, and genetically modified cell lines of the present invention (see, for example, page 19, lines 17-31 of the specification).

In view of the above discussion, reconsideration and withdrawal of the rejection of claims 2, 3, 6-10, 17-24, and 26 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement, is requested.

Summary

It is respectfully submitted that the pending claims are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted
By
Mueting, Raasch & Gebhardt, P.A.
P.O. Box 581415
Minneapolis, MN 55458-1415
Phone: (612) 305-1220
Facsimile: (612) 305-1228
Customer Number 26813

January 9, 2008
Date

By: Nancy A. Johnson
Nancy A. Johnson
Reg. No. 47,266
Direct Dial (612) 305-4723

CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to **Mail Stop Amendment**, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 9 day of January, 2008, at 1:25 pm (Central Time).

By: Sandy Truehart
Name: Sandy Truehart